EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 November 2021

COVID-19 vaccine safety update

COMIRNATY

BioNTech Manufacturing GmbH

The safety of Comirnaty is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 6 October 2021.

Main outcomes from PRAC's latest safety assessment

There are no updates to the product information.

Further assessment of myocarditis and pericarditis is ongoing.

There is currently insufficient evidence of a possible link between Comirnaty and very rare cases of multisystem inflammatory syndrome (MIS).

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Comirnaty are available at Comirnaty: safety updates.

Since its marketing authorisation in the European Union (EU) on 21 December 2020 until 29 October 2021, almost 428 million doses of Comirnaty have been administered in the EU/EEA[1].

1. Updates on safety assessments for Comirnaty

During its meeting held 25 to 28 October 2021, PRAC assessed new safety data for Comirnaty (see section 2 'How safety is monitored').

Myocarditis and pericarditis

PRAC is assessing further data on the risk of myocarditis and pericarditis following vaccination with Comirnaty.

Myocarditis and pericarditis are inflammatory conditions of the heart. Symptoms can vary but often include breathlessness, a forceful heartbeat that may be irregular (palpitations), and chest pain.

PRAC had previously reviewed cases of myocarditis and pericarditis spontaneously reported in the European Economic Area (EEA). The review concluded in July 2021 with a recommendation to list both conditions as side effects in the product information for Comirnaty, together with a warning to raise awareness among healthcare professionals and people receiving this vaccine.

PRAC has now asked the company that markets Comirnaty to perform an in-depth review of all published data on the association of myocarditis and pericarditis with the vaccine, including clinical trial data, data from the literature and other data available in the public domain.

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

Multisystem inflammatory syndrome (MIS)

PRAC has concluded that there is currently insufficient evidence of a possible link between Comirnaty and very rare cases of multisystem inflammatory syndrome (MIS).

MIS is a rare serious inflammatory condition affecting many parts of the body, and symptoms can include tiredness, persistent severe fever, diarrhoea, vomiting, stomach pain, headache, chest pain and difficulty breathing. MIS has previously been reported following COVID-19 disease.

The committee's assessment is based on available spontaneously reported adverse events and currently does not warrant an update of the product information. Only a small number cases met the diagnostic criteria for MIS. Since other infections that could trigger MIS (including COVID-19) could not be fully excluded in all cases, PRAC concluded there is currently insufficient evidence of a possible link with Comirnaty.

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Comirnaty is collected and promptly reviewed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes Monthly Summary Safety Reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing (afterwards, pandemic summary safety reports may cover time periods longer than a month). These reports complement the submission of Periodic Safety Update Reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system. Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including

the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports in all EU/EEA languages. Search for "COVID-19 mRNA Vaccine PFIZER-BIONTECH (Tozinameran)" to see all suspected side effect cases reported for Comirnaty.

As of 28 October 2021, a total of 412,571 cases of suspected side effects with Comirnaty were spontaneously reported to EudraVigilance from EU/EEA countries; 5,520 of these reported a fatal outcome[2,3]. By the same date almost 428 million doses of Comirnaty had been given to people in the EU/EEA[4].

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment. EMA's detailed assessments take into account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Planned and ongoing studies

The company that markets Comirnaty will continue to provide results from the main clinical trial, which is ongoing for up to two years. It will also conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice.

[2] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).
[3] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effects. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.
[4] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

For the list of planned and ongoing safety studies for Comirnaty, see the risk management plan.

A paediatric investigation plan (PIP) for Comirnaty is in place. This describes how the company collects data on the vaccine's efficacy and safety for its use in children.

In addition, EMA is coordinating observational studies in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

3. Other information for Comirnaty

Comirnaty is a vaccine that was authorised in the EU on 21 December 2020 to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death. The initial marketing authorisation was for use in people aged 16 years and older; on 31 May 2021, the marketing authorisation was extended to use in individuals aged 12 years and older.

Comirnaty contains a molecule called mRNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The mRNA is broken down shortly after vaccination. The spike protein does not cause COVID-19.

Before Comirnaty was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 18,000 participants had been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for Comirnaty are usually mild or moderate and get better within a few days after vaccination.

More information on how Comirnaty works and its use is available in all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

European Medicines Agency
Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact
Telephone +31 (0)88 781 6000

© European Medicines Agency, 2021. Reproduction is authorised provided the source is acknowledged.

An agency of the European Union